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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/501,450	05/18/2005	Deepak Bahl	RLL-234US	9397

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EXAMINER	
THOMAS, TIMOTHY P	

ART UNIT	PAPER NUMBER
1609	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/501,450	BAHL ET AL.	
	Examiner	Art Unit	
	Timothy P. Thomas	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *14-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/18/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-13, drawn to a stable pharmaceutical composition.

Group II, claim(s) 14-17, drawn to a process of preparing a stable pharmaceutical composition.

Group III, claim(s) 18, drawn to a method of treating a disorder.

2. The inventions listed as Groups I-III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the technical feature common to the claims is a composition with a core with a seal coat coated with a layer of an ACE inhibitor; the outer ACE inhibitor layer is free of plasticizers and organic solvents. Zerbe (US 4,800,084) teaches a product with all of these components: figure 2 shows the layers, the core made of sugar crystals is tightly sealed by the insulating coat made of ethyl cellulose; the active substance is contained in the depository coating, (column 3, lines 25-40); captopril (an ACE inhibitor) is taught as an active ingredient (column 2, line 64); example 1 outlines a sugar ball core tightly sealed with an adhesive polymer; the depository layer contains water, active ingredient and an adhesive polymer, hence the depository coating is free of plasticizers and organic solvents. Since the technical feature is taught, no special technical feature is present to unify the claims. Therefore, restriction is proper.

3. During a telephone conversation with Jay Deshmukh on 5/24/2007 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-13.

Affirmation of this election must be made by applicant in replying to this Office action.

Claims 14-18 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

4. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is not clear whether the claimed invention requires 4 layers (5 layers when considering claim 13) or only 3 layers (4 layers when considering claim 13). Claim 1 has three numbered components comprising the composition: (i) "a core; coated with a layer of ACE inhibitor(s)"; (ii) "a seal coat on the core" and (iii) "an ACE inhibitory layer which is free of plasticizers and organic solvents". It is not clear whether applicant intended the coating layer of ACE inhibitor(s), specified in (i) to be considered a part of the core, and thus to be placed under the seal coat, which is a separate layer from that specified in (iii) or alternatively, the layer of ACE inhibitor(s), mentioned in (i) is actually intended to be a reference to the layer of (iii). In view of the example compositions in

the specification it appears that applicant intends the latter case; however, the introduction of a film-forming polymer to the layer of ACE inhibitor(s), specified in claims 3-4, seems to support the former case.

In view of the arguments above, references to "the layer of ACE inhibitor(s)" in claim 3 and "the ACE inhibitor layer" of claim 13 are also indistinct; it is not clear which ACE inhibitor layer(s) applicant is referring to.

Claim 9 refers to " a pharmaceutically active substance other than the one which is susceptible to degradation by mechanical stress". It is not clear which "one" substance applicant is referring to. The active compounds with the claimed property are not defined in the claims or the specification; some examples, such as specific ACE Inhibitors have been listed, but it is clear applicant intended to encompass other unspecified compounds by this phrase (e.g., page 3, lines 3-7).

7. Claim 9 recites the limitation "the one [a pharmaceutically active substance] which is susceptible to degradation by mechanical stress" in the second line. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1, 3-6, 8, 11-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Zerbe (US 4,800,084).

Zerbe teaches a pharmaceutical composition for oral administration, comprised of the components of the instant claims (column 2, line 12; figure 2): a pellet core, comprised of sugar crystals or sugar balls (column 3, line 26, 48); which is tightly sealed with an insulating coating made of ethyl cellulose, polyvinyl pyrrolidon[e], hydroxyl propyl methyl cellulose or hydroxyl propyl cellulose (column 3, lines 27-28; column 2, lines 46-57); a depository coating containing an active substance, e.g., especially captopril (an ACE inhibitor; column 3, lines 30-31, column 2, lines 61-64); and an outer coating surrounding the depository coating, comprised of ethyl cellulose, polyvinyl pyrrolidon[e], hydroxyl propyl methyl cellulose or hydroxyl propyl cellulose (column 2, lines 46-57). Example 1 teaches an external layer comprised of active ingredient, lactose, water and hydroxypropyl cellulose (i.e., active layer comprising film forming polymer, free of plasticizers and organic solvents) (column 3, lines 59-62). A pharmaceutically inert material is taught for the core (column 4, lines 17-18). The use of the term pellet implies a compressed tablet is used for the core; Rudnic teaches that a pellet is a material formed by compressing a medicated mass (Remington: The Science and Practice of Pharmacy, Vol II, 19th Ed., 1995, p. 1648; "Pellets").

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 1-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zerbe (US 4,800,084) in view of Bauer et al (US 6,086,919).

Zerbe teaches the components of the claims as outlined above. Zerbe does not teach the ACE inhibitor compounds listed in claim 2, nor a second active, non-ACE inhibitor substance in the core selected from the group listed in claim 10. Bauer teaches pharmaceutical compositions containing dihydropyridine compounds (e.g., feldopine, nitrendipine, nifedipine or lacidipine) and the ACE Inhibitor ramipril combined in an oral dosage form (title; abstract; column 1, lines 11-12, 18-19); a specific

embodiment taught was prepared with felodipine (or any of the other dihydropyridine compounds) in a tablet core compressed using a tabletting machine, then coated with a layer containing ramipril and in a spray or alternative coating method (example 10; column 5, lines 3-6); a compressed tablet core filled in a hard gelatin capsule is taught as an alternative embodiment (example 9); an unspecified inactive layer(s) between the two active agents is taught (Figure 3B; column 16, lines 23-26); however, Bauer does not make clear that this is a coat that seals the formulation. Bauer also does not teach the ramipril coat prepared without organic solvents; ethanol (an organic solvent) is used in example 10. It would be obvious to one of ordinary skill in the art to modify the formulation of Zerbe to include any one of the Bauer dihydropyridine compounds in the core and to include ramipril in the ACE inhibitor layer, or alternatively to place the dihydropyridine containing core material with ACE inhibitor layer together into hard gelatin capsules where the capsule forms an outer protecting coat. The motivation to combine a dihydropyridine compound in the core and ramipril as an outer layer is taught by Bauer, "the choice of an instant release formulation of the long acting ramipril and an extended release preparation of a dihydropyridine both contribute to the optimal use of both drugs, minimizing adverse effects while still being effective against elevated against blood pressure" (column 2, line 64-column 3, line 2). The motivation to place the ramipril-containing formulation into hard gelatin capsules would protect the active agent, which Bauer teaches is sensitive to moisture or compression, and needs special attention to retain stability (column 1, lines 60-63).

Conclusion

14. None of the claims are allowed. Claims 1-13 are rejected; claims 14-18 are withdrawn.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy P. Thomas whose telephone number is (571) 272-8994. The examiner can normally be reached on Monday-Thursday 6:30 a.m. - 5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisors, Cecilia Tsang or Janet Andres can be reached on (571) 272-0562 or (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ardin H. Marschel 6/11/07
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER

/TPT/
Timothy P. Thomas
Patent Examiner